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Search Strategy

FILE 'USPATFULL' ENTERED AT 22:39:32 ON 12 AUG 2002

		E	DE LEYS ROBERT/IN
L1	10	S	E3
		E	ZHENG JIAN/IN
L2	1	S	E3
L3	17619	S	(HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L4	928	S	L3 AND (GP41)
L5	925	S	L4 AND (ANT70 OR ANT?)
L6	12	S	L5 AND (CONCENSUS)

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		E	DE LEYS R/AU
L7	4	S	E3 OR E4
		E	ZHENG J/AU
L8	401	S	E3
L9	16	S	L8 AND (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L10	119158	S	(HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L11	18	S	L10 AND (ANT70 OR TYPE O)

L1 ANSWER 1 OF 10 USPATFULL
2001:116806 HIV-3 retrovirus and its use.
De Leys, Robert, Grimbergen, Belgium
Vanderborght, Bart, Geel, Belgium
Saman, Eric, Niklaas, Belgium
Van Heuverswyn, Hugo, Laarne, Belgium
Innogenetics N.V., Ghent, Belgium (non-U.S. corporation)
US 6265200 B1 20010724
APPLICATION: US 1999-379270 19990823 (9)
PRIORITY: EP 1988-109200 19880609
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described is a new variety of retrovirus designated HIV-3, also known as HIV-1 subtype O, samples of which are deposited in the European Collection of Animal Cell Cultures (ECACC) under V88060301. Further described are variants of the virus.

CLM What is claimed is:
1. A variant of HIV-3 retrovirus, comprising three core proteins with molecular weights of about 12 kD, about 17 kD, and about 25 kD, an endonuclease with molecular weight of about 31 kD, two reverse trascnriptases with molecular weights of about 49 kD and about 62 kD, a transmembrane protein with molecular weight of about 41 kD, and an outer membrane protein with molecular weight of about 120 kD, the variant characterized in that its RNA does not hybridize with RNA or DNA derived from either the Env gene, the LTR sequence, or the Pol region of the HIV-1 genome, under stringent conditions.

2. A variant of HIV-3 retrovirus, comprising three core proteins with molecular weights of about 12 kD, about 17 kD, and about 25 kD, an endonuclease with molecular weight of about 31 kD, two reverse transcriptases with molecular weights of about 49 kD and about 62 kD, a transmembrane protein with molecular weight of about 41 kD, and an outer membrane protein with molecular weight of about 120 kD, the variant characterized in that its LTR sequence is about 70% or less homologous to the LIR sequence of HIV-1 and less than 55% homologous to the LTR sequence of HIV-2.

L1 ANSWER 2 OF 10 USPATFULL
2001:47777 Peptide derived from human immunodeficiency virus type 1 (HIV-1), isolate Ant70, containing an immunodominant epitope and it's use in immunodiagnostic assays.
De Leys, Robert, Grimbergen, Belgium
N. V. Innogenetics S. A., Ghent, Belgium (non-U.S. corporation)
US 6210903 B1 20010403
APPLICATION: US 1998-112206 19980709 (9)
PRIORITY: EP 1992-400598 19920306
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention is directed toward a peptide corresponding to an immunologically important viral epitope. Specifically, the peptide corresponds to an immunodominant epitope identified in the gp120 region of the human immunodeficiency virus type 1 (HIV-1), strain Ant70. This peptide has the following amino acid sequence: NH.sub.2 -Gln-Ile-Asp-Ile-Gln-Glu-Met-Arg-Ile-Gly-Pro-Met-Ala-Trp-Tyr-Ser-Met-Gly-Ile-Gly-Gly-CO.sub.2 H. The invention also relates to the use of this peptide, particularly when biotinylated in the form of complexes of

streptavidin-biotinylated peptides or of avidin-biotinylated peptides, for the in vitro determination of HIV-1-specific antibodies.

CLM What is claimed is:

1. A peptide having the amino acid sequence set forth in SEQ ID NO:162 and the following chemical structure: (A) (B) (X) Y Gln-Ile-Asp-Ile-Gln-Glu-Met-Arg-Ile-Gly-Pro-Met-Ala-Trp-Tyr-Ser-Met-Gly-Ile-Gly-GlyY (X) (Z); wherein B represents biotin, X represents a biotinylation compound which is incorporated during the synthetic process, Y represents a covalent bond or a linker arm, A represents at least one amino acid, amino group, or chemically modified amino terminus of the peptide, Z represents at least amino acid, OH-group, NH.sub.2 -group or a linkage involving these two groups, and the parentheses indicate that the presence of any given group in this position is optional.

2. The peptide of claim 1 wherein Y is selected from the group consisting of a glycine reside, .beta. alanine, 4-aminobutyric acid, 5-amino valeric acid and 6-aminohexanoic acid.

3. A peptide having an amino acid sequence consisting of: Gln-Ile-Asp-Ile-Gln-Glu-Met-Arg-Ile-Gly-Pro-Met-Ala-Trp-Tyr-Ser-Met-Gly-Ile-Gly-Gly (SEQID NO:162).

4. The peptide according to claim 1, wherein said peptide is biotinylated N-terminally, C-terminally or internally.

5. The peptide according to claim 4 which is coupled to streptavidin or avidin, with said streptavidin or avidin optionally coupled to a solid phase.

6. The peptide according to claim 1, with said peptide being anchored to a solid support via covalent or non-covalent bonds.

7. An immunoassay process for determining the presence of antibodies to HIV in a biological sample using a peptide according to claim 1, the process comprising: contacting the biological sample with a composition comprising the peptide according to claim 1, and detecting any immune complex formed between said antibodies and said peptide.

8. An immunological assay kit for detecting antibodies to HIV comprising a peptide according to claim 1.

9. A Line immunoassay kit for detecting antibodies to HIV comprising a peptide according to claim 6.

L1 ANSWER 4 OF 10 USPATFULL
2000:156965 Peptides for the detection of HIV-1 group O.
De Leys, Robert, Three Bridges, NJ, United States
Zheng, Jian, Raritan, NJ, United States
Ortho-Clinical Diagnostics, Inc., Rochester, NY, United States (U.S. corporation)
US 6149910 20001121
APPLICATION: US 1999-433428 19991104 (9)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to peptides and their preparation. The peptides each have a sequence that corresponds to the immunodominant region of the HIV-1 group O gp41 envelope protein. The sequence is characterized in that it does not correspond to any known naturally occurring group O

sequence or variant. Furthermore, the peptide binds anti-HIV-1 group O antibodies. There are several uses for the peptides, including the detection of antibodies produced in response to HIV-1 group O infection. The peptides may also be incorporated in mosaics and expressed recombinantly.

CLM What is claimed is:
1. A peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:59
NQQRLNSWGCKGRIICYTSARWH,
SEQ ID NO;61
EQQRLNSWGCKGRIICYTSARWH,
SEQ ID NO:69
GRETLMQDQQRLNSWGCKGRIICYTSARWH,
SEQ ID NO:60
XQQRLNSWGCKGRIICYTSARWH,
SEQ ID NO:62
ETLMQXQQRLNSWGCKGRIICYTSARWH,
SEQ ID NO:64
RARLQALETLMQNQQRLNSWGCKGRIICYTSARWH, and
SEQ ID NO:65
DQQVNNVSSIIYDKILEAQDQQEENVRELLELD.

2. The peptide of claim 1 wherein said peptide binds anti-HIV group O antibodies.

3. The peptide of claim 1 wherein said peptide is made by recombinant or synthetic chemistry methods.

L1 ANSWER 5 OF 10 USPATFULL
2000:4647 HIV-3 retrovirus and its use.
De Leys, Robert, Grimbergen, Belgium
Vanderborght, Bart, Geel, Belgium
Saman, Eric, St. Niklaas, Belgium
Van Heuverswyn, Hugo, Laarne, Belgium
Innogenetics N.V., Ghent, Belgium (non-U.S. corporation)
US 6013484 20000111
APPLICATION: US 1997-900902 19970725 (8)
PRIORITY: EP 1988-109200 19880609
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described is a new variety of retrovirus designated HIV-3, samples of which are deposited in the European Collection of Animal Cell Cultures (ECACC) under V88060301. Further described are antigens obtained from the virus, particularly proteins p12, p16, p25 and glycoproteins gp41 and gp120 to be used in the diagnosis of ARC or AIDS caused by HIV-3. Immunogenic compositions to be used as vaccines contain an envelope glycoprotein of HIV-3 such as gp41 or gp120.

CLM What is claimed is:
1. A process for making a monoclonal antibody that recognizes a protein or glycoprotein antigen of HIV-3 retrovirus (also known as HIV-1 subtype O virus), said retrovirus having the morphological and immunological characteristics of any of the retroviruses deposited in the European Collection of Animal Cell Cultures under V88060301, the process comprising: (a) infecting an animal with at least one antigen selected from a protein or a glycoprotein of HIV-3 to form antibody-producing cells; (b) fusing said antibody-producing cells with immortalized cells

under hybridoma-forming conditions to form hybridomas; (c) selecting at least one hybridoma which secretes monoclonal antibodies which recognize the antigen as determined by western blot or by ELISA; and, (d) collecting monoclonal antibodies secreted by the hybridoma.

2. The process of claim 1, wherein the antigen is a protein lysate of HIV-3.

3. The process of claim 1, wherein the antigen is an internal core protein of HIV-3 selected from the group consisting of p12, p16, p25, and mixtures thereof.

4. The process of claim 1, wherein the antigen is an envelope glycoprotein of HIV-3 selected from the group consisting of gp41, gp120, and mixtures thereof.

5. A process for making a monoclonal antibody that recognizes a protein or glycoprotein antigen of HIV-3 retrovirus (also known as HIV-1 subtype O virus), said retrovirus having the morphological and immunological characteristics of any of the retroviruses deposited in the European Collection of Animal Cell Cultures under V88060301, the process comprising: (a) immortalizing B-cells derived from persons infected with HIV-3, at least one said B-cell secreting monoclonal antibodies which recognize a protein or glycoprotein of HIV-3 as determined by western blot or by ELISA; and, (b) collecting monoclonal antibodies secreted by the B-cell.

6. The process of claim 5, wherein the protein or the glycoprotein of HIV-3 is a protein lysate of HIV-3.

7. The process of claim 5, wherein the protein or the glycoprotein of HIV-3 is an internal core protein of HIV-3 selected from the group consisting of p12, p16, and p25.

8. The process of claim 5, wherein the protein or the glycoprotein of HIV-3 is an envelope glycoprotein of HIV-3 selected from the group consisting of gp41 and gp120.

9. In a process for producing monoclonal antibodies, the improvement comprising preparing monoclonal antibodies against at least one antigen selected from a protein or a glycoprotein of HIV-3 retrovirus (also known as HIV-1 subtype O virus), said retrovirus having the morphological and immunological characteristics of any of the retroviruses deposited in the European Collection of Animal Cell Cultures under V88060301.

10. The process of claim 9, wherein the antigen is a protein lysate of HIV-3.

11. The process of claim 9, wherein the antigen is an internal core protein of HIV-3 selected from the group consisting of p12, p16, p25, and mixtures thereof.

12. The process of claim 9, wherein the antigen is an envelope glycoprotein of HIV-3 selected from the group consisting of gp41, gp120, and mixtures thereof.

L1 ANSWER 6 OF 10 USPATFULL
1999:43388 Peptide derived from human immunodeficiency virus type 1 (HIV-1), isolate ant70, containing an immunodominant epitope and it's use in

immunodiagnostic assays.
De Leys, Robert, Grimbergen, Belgium
N.V. Innogenetics S.A., Ghent, Belgium (non-U.S. corporation)
US 5891640 19990406
WO 9318054 19930916
APPLICATION: US 1993-146028 19931122 (8)
WO 1993-EP517 19930308 19931122 PCT 371 date 19931122 PCT 102(e) date
PRIORITY: EP 1992-400598 19920306
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention is directed toward a peptide corresponding to an immunologically important viral epitope. Specifically, the peptide corresponds to an immunodominant epitope identified in the gp41 region of the human immunodeficiency virus type 1 (HIV-1), strain Ant70. This peptide has the following amino acid sequence: NH.sub.2 -Leu-Trp-Gly-Cys-Lys-Gly-Lys-Leu-Val-Cys-CO.sub.2 H. The invention also relates to the use of this peptide, particularly when biotinylated in the form of complexes of streptavidin-biotinylated peptides or of avidin-biotinylated peptides, for the in vitro determination of HIV-1-specific antibodies.

CLM What is claimed is:
1. A peptide having the amino acid sequence set forth in SEQ ID NO: 5 and the following chemical structure: (A) (B) (X) Y-Leu Trp Gly Cys Lys Gly Lys Leu Val Cys-Y (X) (Z); wherein B represents biotin, X represents a biotinylation compound which is incorporated during the synthetic process, Y represents a covalent bond or a linker arm separating the peptide from the biotinyl moiety of B, A represents at least one amino acid, amino group, or chemically modified amino terminus of the peptide, Z represents at least one amino acid, OH-group, NH2-group, or a linkage involving these two groups, and parentheses indicate that the presence of any given group in this position is optional.

2. The peptide of claim 1 wherein Y is selected from the group consisting of a glycine residue, .beta. alanine, 4-aminobutyric acid, 5-amino valeric acid and 6-aminohexanoic acid.

3. The peptide according to claim 1 having an amino acid sequence consisting of: Leu Trp Gly Cys Lys Gly Lys Leu Val Cys (SEQ ID NO: 5).

4. The peptide according to claim 1, wherein said peptide is biotinylated N-terminally, C-terminally or internally.

5. The peptide according to claim 4 which is coupled to streptavidin or avidin, with said streptavidin or avidin optionally coupled to a solid phase.

6. The peptide according to claim 1, with said peptide being anchored to a solid support via covalent or non-covalent bonds.

7. An immunoassay process for determining the presence of antibodies to HIV in a biological sample using a peptide according to claim 1, the process comprising: contacting the biological sample with a composition comprising the peptide according to claim 1, and detecting any immune complex formed between said antibodies and said peptide.

8. An immunological assay kit for detecting antibodies to HIV comprising a peptide according to claim 1.

9. A Line immunoassay kit for detecting antibodies to HIV comprising a

peptide according to claim 6.

L1 ANSWER 7 OF 10 USPATFULL
1999:4316 Methods for detecting antibodies against HIV-3 retrovirus [and its use].
De Leys, Robert, Grimbergen, Belgium
Vanderborght, Bart, Geel, Belgium
Saman, Eric, Niklaas, Belgium
Van Heuverswyn, Hugo, Laarne, Belgium
Innogenetics N.V., Ghent, Belgium (non-U.S. corporation)
US 5858647 19990112
APPLICATION: US 1995-474360 19950607 (8)
PRIORITY: EP 1988-109200 19880609
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described is a new variety of retrovirus designated HIV-3, samples of which are deposited in the European Collection of Animal Cell Cultures (ECACC) under V88060301. Further described are antigens obtained from the virus, particularly proteins p12, p16, p25 and glycoproteins gp41 and gp120 to be used in the diagnosis of ARC or AIDS caused by HIV-3. The methods to detect antibodies against HIV-3 retrovirus in a biological fluid involve contacting the suspect body fluid with a composition containing one or more of the proteins or glycoproteins of HIV-3 or with a lysate of the virus, or with an antigen possessing epitopes common to HIV-3, and detecting the immunological conjugate formed between the anti-HIV-3 antibodies and the antigen(s) used.

CLM What is claimed is:
1. A method for the detection of antibodies against HIV-3 retrovirus (also known as HIV-1 subtype O virus) in a biological fluid to assist in the diagnosis of a potential or existing ARC or AIDS caused by said HIV-3 retrovirus comprising: (a) collecting a biological fluid from a human subject; (b) providing a control sample; (c) contacting the biological fluid with a composition comprising at least one purified or isolated antigen of HIV-3 retrovirus having the morphological and immunological characteristics of any of the retroviruses deposited in the European Collection of Animal Cell Cultures (ECACC) under V88060301; and (d) detecting the immunological conjugate formed between the antigen used and the antibodies present in the biological sample, and comparing the detection signal obtained with the human sample to the control sample.

2. The method of claim 1 wherein the composition comprises at least one of the internal core proteins of said retrovirus, in particular p12, p16 or p25 having apparent molecular weights in the order of 12,000, 16,000 and 25,000, respectively.

3. The method of claim 1 wherein the composition comprises at least one of the envelope proteins of said retrovirus, in particular gp41 or gp120 having apparent molecular weights in the order of 40,000-45,000 and 120,000, respectively.

4. The method of claim 1 wherein the composition comprises the p12 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the p12 protein from the gel.

5. The method of claim 1 wherein the composition comprises the p16 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the p16 protein from the gel.

6. The method of claim 1 wherein the composition comprises the p25 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the p25 protein from the gel.

7. The method of claim 1 wherein the composition comprises the gp41 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the gp41 protein from the gel.

8. The method of claim 1 wherein the composition comprises the gp120 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the gp120 protein from the gel.

9. The method of claim 1 wherein the biological fluid is serum or spinal fluid.

10. A kit for the detection of anti-HIV-3-antibodies in a biological fluid comprising at least one isolated or purified antigen of HIV-3 retrovirus (also known as HIV-1 subtype O virus) (ECACC V88060301), a control sample, and reagents for detecting the immunological complex formed between the isolated or purified HIV-3 antigens, or the control sample, and the antibodies present in the biological sample.

11. The kit of claim 10 wherein the composition comprises at least one of the internal core proteins of said retrovirus, in particular p12, p16 or p25 having apparent molecular weights in the order of 12,000, 16,000 and 25,000, respectively.

12. The kit of claim 10 wherein the composition comprises at least one of the envelope proteins of said retrovirus, in particular gp41 or gp120 having apparent molecular weights in the order of 40,000-45,000 and 120,000, respectively.

13. The kit of claim 10 wherein the antigen is the p12 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the p12 protein from the gel.

14. The kit of claim 10 wherein the antigen is the p16 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the p16 protein from the gel.

15. The kit of claim 10 wherein the antigen is the p25 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the p25 protein from the gel.

16. The kit of claim 10 wherein the antigen is the gp41 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the gp41 protein from the gel.

17. The kit of claim 10 wherein the antigen is the gp120 protein of HIV-3 obtained by subjecting an HIV-3 viral extract or lysate to gel electrophoresis, and isolating the gp120 protein from the gel.

L1 ANSWER 8 OF 10 USPATFULL
1998:98770 HIV-3 retrovirus antigen compositions.
De Leys, Robert, Grimbergen, Belgium
Vanderborght, Bart, Geel, Belgium
Saman, Eric, St. Niklaas, Belgium
Van Heuverswyn, Hugo, Laarne, Belgium
Innogenetics N.V., Ghent, Belgium (non-U.S. corporation)

US 5795743 19980818
APPLICATION: US 1995-486836 19950607 (8)
PRIORITY: EP 1988-109200 19880609
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described is a new variety of retrovirus designated HIV-3 samples of which are deposited in the European Collection of Animal Cell Cultures (ECACC) under V88060301. Further described are antigens obtained from the virus, particularly proteins p12, p16, p25 and glycoproteins gp41 and gp120 to be used in the diagnosis of ARC or AIDS caused by HIV-3. Immunogenic compositions to be used as vaccines contain an envelope glycoprotein of HIV-3 such as gp41 or gp120.

CLM What is claimed is:

1. A composition comprising at least one protein or glycoprotein of HIV-3 retrovirus, said retrovirus (also known as HIV-1 subtype O virus) having the morphological and immunological characteristics of any of the retroviruses deposited in the European Collection of Animal Cell Cultures under V88060301.

2. The composition of claim 1 wherein the composition comprises a total extract or lysate of HIV-3 retrovirus.

3. The composition of claim 1 wherein the composition comprises at least one of the internal core proteins of HIV-3 retrovirus selected from the group consisting of p12, p16 and p25.

4. The composition of claim 1 wherein the composition comprises at least one of the envelope glycoproteinsof HIV-3 retrovirus selected from the group consisting of gp41 and gp120.

5. A purified antigen of HIV-3 retrovirus (also known as HIV-1 subtype O virus) providing a single band in polyacrylamide gel electrophoresis, and containing an epitope that is immunoreactive with patient sera containing anti-HIV-3 antibodies.

6. A purified antigen selected from the group consisting of p12, p16, p25, gp41 and gp120, wherein the antigen is isolated from HIV-3 retrovirus (also known as HIV-1 subtype O virus).

7. The antigen of claim 6 wherein the antigen is the p12 protein of HIV-3, obtained by subjecting an extract or lysate of HIV-3 to gel electrophoresis and isolating the p12 protein from the gel.

8. The antigen of claim 6 wherein the antigen is the p16 protein of HIV-3, obtained by subjecting an extract or lysate of HIV-3 to gel electrophoresis and isolating the p16 protein from the gel.

9. The antigen of claim 6 wherein the antigen is the p25 protein of HIV-3, obtained by subjecting an extract or lysate of HIV-3 to gel electrophoresis and isolating the p25 protein from the gel.

10. The antigen of claim 6 wherein the antigen is the gp41 protein of HIV-3, obtained by subjecting an extract or lysate of HIV-3 to gel electrophoresis and isolating the gp41 protein from the gel.

11. The antigen of claim 6 wherein the antigen is the gp120 protein of HIV-3, obtained by subjecting an extract or lysate of HIV-3 to gel electrophoresis and isolating the gp120 protein from the gel.

12. A method for the production of antigens of HIV-3 retrovirus (also known as HIV-1 subtype O virus) comprising the steps of lysing the retrovirus and recovering the lysate containing HIV-3 antigens.

L1 ANSWER 9 OF 10 USPATFULL
96:96943 HIV-3 retrovirus and its use.
De Leys, Robert, Grimbergen, Belgium
Vanderborght, Bart, Geel, Belgium
Saman, Eric, Niklaas, Belgium
Van Heuverswyn, Hugo, Laarne, Belgium
Innogenetics N.V., Belgium (non-U.S. corporation)
US 5567603 19961022
APPLICATION: US 1994-228519 19940415 (8)
PRIORITY: EP 1988-109200 19880609
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described is a new retrovirus designated HIV-3, samples of which have been deposited in the European Collection of Animal Cell Cultures (ECACC) under V88060301. The morphological and immunological properties exhibited by the HIV-3 retrovirus class include:

a diameter of approximately 120 nm; a tropism for T4 lymphocytes; cultivation in T4 receptor-bearing immortalized cell lines; cytotoxicity for the lymphocytes that it infects; a magnesium dependent reverse transcriptase activity;

the genomic RNA of HIV-3 hybridizes neither with the sequences of HIV-1 nor with the sequences of HIV-2 under stringent hybridization conditions;

lysates of the virus contain a p25 protein which is immunologically distinct from the p19 protein of HTLV-I and the p24 proteins of HIV-1 and HIV-2 as determined by Western blot analysis, respectively;

lysates of the virus contain a gp120 protein which is immunologically distinct from the gp110 protein of HTLV-I, the gp120 of HIV-1 and the gp120 of HIV-2 as determined by Western blot analysis;

the lysate of the virus contains in addition a gp41 glycoprotein with a molecular weight of 40,000-45,000; and

lysates of the virus contain a p12 protein which is immunologically distinct from the p12 proteins of HIV-1 and HIV-2 as determined by Western blot analysis.

Also described are nucleic acid sequences derived from HIV-3 RNA which can be used as hybridization probes to detect the presence of HIV-3 virus.

CLM What is claimed is:
1. HIV-3 retrovirus or variants of this virus having the essential morphological and immunological properties of any of the retroviruses deposited at the European Collection of Animal Cell Cultures (ECACC) under No. V88060301, said essential morphological and immunological properties are as follows: the virus exhibits a tropism for T4 lymphocytes; the virus is cytotoxic for the lymphocytes that it infects; the virus has a diameter of approximately 120 nm; the virus possesses a magnesium dependent reverse transcriptase activity; the virus can be cultivated in T4 receptor-bearing immortalized cell lines; lysates of

the virus contain a p25 protein which is immunologically distinct from the p19 protein of HTLV-I and the p24 proteins of HIV-1 and HIV-2 as determined by Western blot analysis, respectively; lysates of the virus contain a gp120 protein which is immunologically distinct from the gp110 protein of HTLV-I, the gp120 of HIV-1 and the gp120 of HIV-2 as determined by western blot analysis; the lysate of the virus contains in addition a gp41 glycoprotein with a molecular weight of 40,000-45,000; the genomic RNA of HIV-3 hybridizes neither with the sequences of HIV-1 nor with the sequences of HIV-2 under stringent hybridization conditions; and lysates of the virus contain a p12 protein which is immunologically distinct from the p12 proteins of HIV-1 and HIV-2 as determined by Western blot analysis.

2. The retrovirus of claim 1 characterized in that its RNA virtually hybridizes neither with the Env gene and the LTR close to it of HIV-1, in particular not with the nucleotide sequence 8352-9538 of HIV-1, nor with the sequences of the Pol region of the HIV-1 genome under stringent conditions.

3. A process for the production of the retrovirus of claim 1 characterized by culturing human T4 lymphocytes, or permanent cell lines derived therefrom carrying the T4 phenotype, with lymphocytes or cell lines that have previously been infected with an isolate of said retrovirus, as well as recovering and purifying the retrovirus from the culture medium.

4. A process for the production of any of the proteins or glycoproteins p12, p16, p25, gp41 and gp120 of the retrovirus of claim 1 comprising: inserting the corresponding nucleic acid sequence of said retrovirus in an expression vector, transforming a host with said vector, culturing the transformed host as well as recovering and purifying the expressed protein.

5. The retrovirus of claim 1 having genomic RNA which hybridizes neither with the sequences of HIV-1 nor with the sequences of HIV-2 under stringent hybridization conditions, said genomic RNA comprising an LTR region also comprises a nucleotide sequence which hybridizes under stringent conditions with the following nucleotide sequence:

```
10        20        30        40        50        60
CCCATGGATT
          TGAAGATACA
                    CATAAAGAAA
                              TACTGATGTG
                                        GAAGTTTGAT
                                                  AGATCTCTAG
70        80        90        100       110       120
GCAACACCCA
          TGTTGCTATG
                    ATAACTCACC
                              CAGAGCTCTT
                                        CCAGAAGGAC
                                                  TAAAAACTGC
130       140       150       160       170       180
TGACCTGAAG
          ATTGCTGACA
                    CTGTGGAACT
                              TTCCAGCAAA
                                        GACTGCTGAC
                                                  ACTGCGGGGA
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190       200       210       220       230       240
CTTTCCAGTG
          GGAGGGACAG
                    GGGGCGGTTC
                              GGGGAGTGGC
                                        TAACCCTCAG
                                                  AAGCTGCATA
250       260       270       280       290       300
TAAGCAGCCG
          CTTTCTGCTT
                    GTACCGGGTC
                              TCGGTTAGAG
                                        GACCAGGTCT
                                                  GAGCCCGGGA
310       320       330       340       350       360
GCTCCCTGGC
          CTCTAGCTGA
                    ACCCGCTCGT
                              TAACGCTCAA
                                        TAAAGCTTGC
                                                  CTTGAGTGAG
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A.

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6. The retrovirus of claim 1 having genomic RNA which hybridizes neither with sequences of HIV-1 nor with the sequences of HIV-2 under stringent hybridization conditions, said genomic RNA also comprises a nucleotide sequence which hybridizes under stringent conditions with the following nucleotide sequence:

```
10        20        30        40        50        60
AACATGGGAA ACGCATTGAG
                    AAAAGGTAAA
                              TTTGAGGGAT GGGCAGCAGT
                                                  AAGAGAAAGA
70        80        90        100       110       120
ATGAGAAGAA CTAGAACTTT
                    CCCTGAGTCT
                              GAACCATGCG CACCTGGAGT
                                                  AGGACAGATC
130       140       150       160       170       180
TCCAGGGAAT TAGCAGCTAG
                    AGGAGGGATA
                              CCAAGTTCCC ATACTCCTCA
                                                  AAACAATGCA
190       200       210       220       230       240
GCCCTTGCAT TCCTAGAAAG
                    TCACCAAGAG
                              GAAGAAGTAG GTTTTCCAGT
                                                  AGCACCTCAA
250       260       270       280       290       300
GTGCCTCTAA GGCCAATGAC
                    CTATAAAGGA
                              GCATTTGACC TCAGCTTCTT
                                                  TTTAAAAGAA
310       320       330       340       350       360
AAGGGAGGAC TGGAAGGGTT
                    AATTTACTCC
                              CATAAAAGAG CAGAAATCCT
```

GGATCTTTGG
GTGTATAA.

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7. A nucleotide sequence comprising the entire genomic RNA of the retrovirus of claim 1.

8. A nucleotide sequence comprising cDNA corresponding to the entire genomic RNA of the retrovirus of claim 1.

9. A nucleotide sequence coding for the amino.sub.-- acid sequences of proteins p12, p16 or p25 of the retrovirus of claim 1.

10. A nucleotide sequence coding for the amino.sub.-- acid sequences of glycoproteins gp41 or gp120 of the retrovirus of claim 1.

11. A process for the production of a hybridization probe for the detection of the RNA of the retrovirus of claim 1 comprising: inserting a nucleotide sequence of any of claims 7 to 10 in a cloning vector by in vitro recombination, cloning the modified vector obtained in a suitable cellular host, and recovering the hybridization probe.

12. The nucleotide sequence of any one of claims 7 to 10 which is labelled.

13. A recombinant nucleic acid vector comprising a nucleotide sequence of any one of claims 7 to 10 inserted therein.

14. The retrovirus of claim 1 wherein the LTR sequence of said retrovirus is about 70% or less homologous to the LTR sequence of HIV-1 or HIV-2.

15. A nucleotide sequence identified by the sequence:

```
10          20          30          40          50          60
CCCATGGATT TGAAGATACA
                        CATAAAGAAA TACTGATGTG
                                                GAAGTTTGAT
                                                            AGATCTCTAG
70          80          90          100         110         120
GCAACACCCA TGTTGCTATG
                        ATAACTCACC CAGAGCTCTT
                                                CCAGAAGGAC
                                                            TAAAAACTGC
130         140         150         160         170         180
TGACCTGAAG ATTGCTGACA
                        CTGTGGAACT TTCCAGCAAA
                                                GACTGCTGAC
                                                            ACTGCGGGGA
190         200         210         220         230         240
CTTTCCAGTG GGAGGGACAG
                        GGGGCGGTTC GGGGAGTGGC
                                                TAACCCTCAG
                                                            AAGCTGCATA
250         260         270         280         290         300
TAAGCAGCCG CTTTCTGCTT
                        GTACCGGGTC TCGGTTAGAG
                                                GACCAGGTCT
```

```
                                                                  GAGCCCGGGA
310         320         330         340         350         360
GCTCCCTGGC CTCTAGCTGA
                        ACCCGCTCGT TAACGCTCAA
                                                TAAAGCTTGC
                                                          CTTGAGTGAG
A;
or
10          20          30          40          50          60
AACATGGGAA ACGCATTGAG
                        AAAAGGTAAA TTTGAGGGAT
                                                GGGCAGCAGT
                                                          AAGAGAAAGA
70          80          90          100         110         120
ATGAGAAGAA CTAGAACTTT
                        CCCTGAGTCT GAACCATGCG
                                                CACCTGGAGT
                                                          AGGACAGATC
130         140         150         160         170         180
TCCAGGGAAT TAGCAGCTAG
                        AGGAGGGATA CCAAGTTCCC
                                                ATACTCCTCA
                                                          AAACAATGCA
190         200         210         220         230         240
GCCCTTGCAT TCCTAGAAAG
                        TCACCAAGAG GAAGAAGTAG
                                                GTTTTCCAGT
                                                          AGCACCTCAA
250         260         270         280         290         300
GTGCCTCTAA GGCCAATGAC
                        CTATAAAGGA GCATTTGACC
                                                TCAGCTTCTT
                                                          TTTAAAAGAA
310         320         330         340         350         360
AAGGGAGGAC TGGAAGGGTT
                        AATTTACTCC CATAAAAGAG
                                                CAGAAATCCT
                                                          GGATCTTTGG
GTGTATAA.
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L1 ANSWER 10 OF 10 USPATFULL
94:33132 HIV-3 retrovirus and its use.
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Vanderborght, Bart, Geel, Belgium
Saman, Eric, St. Niklaas, Belgium
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Innogenetics N.V., Belgium (non-U.S. corporation)
US 5304466 19940419
WO 8912094 19891214
APPLICATION: US 1990-460913 19900323 (7)
WO 1989-EP643 19890608 19900323 PCT 371 date 19900323 PCT 102(e) date
PRIORITY: EP 1988-109200 19880609
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described is a new retrovirus designated HIV-3 and deposited in the European Collection of Animal Cell Cultures (ECACC) under V88060301.

Further described are antigens obtained from the virus, particularly proteins p12, p16, p25 and glycoproteins gp41 and gp120 to be used in the diagnosis of ARC or AIDS caused by HIV-3. Immunogenic compositions to be used as vaccines contain an envelope glycoprotein of HIV-3 such as gp41 or gp120.

CLM What is claimed is:

1. A method for detecting antibodies against HIV-3 retrovirus in a body fluid comprising: (a) contacting body of a person to be diagnosed with a composition comprising at least one antigen of said HIV-3 retrovirus, said retrovirus having the morphological and immunological properties of any of the retroviruses deposited at the European Collection of Animal Cell Cultures (ECACC) under N V88060301, including the characteristics that: the virus exhibits a tropism for T4 lymphocytes; the virus is cytotoxic for the lymphocytes that it infects; the virus has a diameter of approximately 120 nm; the virus possesses a magnesium dependent reverse transcriptase activity; the virus can be cultivated in T4 receptor-bearing immortalized cell lines; lysates of the virus contain a p25 protein which is immunologically distinct from the p19 protein of HTLV-I by Western blot analysis; the lysates of the virus contains in addition a glycoprotein with a molecular weight of 40,000-45,000; and the genomic RNA of HIV-3 hybridizes neither with the sequences of HIV-1 nor with the sequence of HIV-2 under stringent hybridization conditions; and (b) detecting an immunological complex formed between said anti-HIV-3 antibodies and the antigen used.

2. The method of claim 1 wherein the tested body fluid is serum or spinal fluid.

3. The method of claim 1 wherein the composition comprises a total extract or lysate of said retrovirus.

4. The method of claim 1 wherein the composition contains a purified antigen, said antigen provided as a single band in polyacrylamide gel electrophoresis, and said antigen comprising an epitope that is recognized by anti-HIV-3 antibodies.

5. The method of claim 4 wherein the purified antigen has the immunological characteristics of an HIV-3 protein or glycoprotein selected from the group consisting of p12, p16, p25, gp41 and gp120.

6. The method of claim 1 wherein the composition contains at least one of the internal core proteins of said retrovirus.

7. The method of claim 6 wherein the internal core protein is selected from the group consisting of p12, p16 and p25 having apparent molecular weights of about 12,000, 16,000 and 25,000, respectively.

8. The method of claim 1 wherein the composition contains at least one of the envelope proteins of said retrovirus.

9. The method of claim 8 wherein the envelope protein is gp41 or gp120 having apparent molecular weights of about 40,000-45,000 and about 120,000, respectively.

10. The method of claim 1, characterized in that said detection of said immunological complex is achieved by reacting said immunological complex with a labeled reagent selected from the group consisting of antihuman immunoglobulin-antibodies, bacterial A protein and bacterial G protein and then detecting the product formed between said complex and said reagent.

11. A kit for detecting anti-HIV-3-antibodies in a body fluid, comprising: (a) a composition comprising at least one protein or glycoprotein antigen of HIV-3 retrovirus having the morphological and immunological properties of any of the retroviruses deposited at the European Collection of Animal Cell Cultures (ECACC) under N V88060301, including the characteristics that: the virus exhibits a tropism for T4 lymphocytes; the virus is cytotoxic for the lymphocytes that it infects; the virus has a diameter of approximately 120 nm. The virus possesses a magnesium dependent reverse transcriptase activity; the virus can be cultivated in T4 receptor-bearing immortalized cell lines; lysates of the virus contain a p25 protein which is immunologically distinct from the p19 protein of HTLV-I by Western blot analysis; lysates of the virus contain in addition a glycoprotein with a molecular weight of 40,000-45,000; and the genomic RNA of HIV-3 hybridizes neither with the sequences of HIV-1 nor with the sequence of HIV-2 under stringent hybridization conditions; and (b) means for detecting the immunological complex formed.

12. The kit of claim 11 wherein the composition comprises a total extract or lysate of said retrovirus.

13. The kit of claim 11 wherein the antigen provides a single band in polyacrylamide gel electrophoresis, said antigen comprising an epitope that is recognized by serum of a patient carrying anti-HIV-3 antibodies.

14. The kit of claim 13 wherein the antigen is a purified antigen having the immunological characteristics of an HIV-3 protein or glycoprotein selected from the group consisting of p12, p16, p25gp41 and gp120.

15. The kit of claim 11 wherein the composition contains at least one of the internal core proteins of said retrovirus.

16. The kit of claim 15 wherein the internal core protein is selected from the group consisting of p12, p16 and p25 having apparent molecular weights of about 12,000, 16,000 and 25,000, respectively.

17. The kit of claim 11 wherein the composition contains at least one of the envelope proteins of said retrovirus.

18. The kit of claim 17 wherein the envelope protein is gp41 or gp120 having apparent molecular weights of about 40,000-45,000 and about 120,000, respectively.

19. The kit of claim 11, which further comprises a labeled reagent selected from the group consisting of antihuman immunoglobin(s), protein A and bacterial G protein.

L7 ANSWER 1 OF 4 MEDLINE
94149849 Document Number: 94149849. PubMed ID: 8107220. Genomic cloning and complete sequence analysis of a highly divergent African human immunodeficiency virus isolate. Vanden Haesevelde M; Decourt J L; De Leys R J; Vanderborght B; van der Groen G; van Heuverswijn H; Saman E. (Innogenetics N.V., Gent, Belgium.) JOURNAL OF VIROLOGY, (1994 Mar) 68 (3) 1586-96. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Analysis of the complete sequence of a human immunodeficiency virus (HIV) isolate (Ant70) obtained from a Cameroonian patient indicates that this virus is the most divergent strain within the HIV-1 family hitherto described. Comparison of the Pol protein, usually highly conserved within the HIV-1 family, shows only about 73% similarity with the HIVmm isolate, whereas for the more variable proteins such as envelope, similarities of 50% or lower are found. The principal neutralizing determinant (V3 loop) and the immunodominant region within gp41 also contain some unusual substitutions, which may have implications for protein function as well as for serological assays based on these regions. Phylogenetic analyses show that this isolate occupies a unique position relative to the human HIV-1 isolates and the recently described SIVcpz virus, indicating that this Cameroonian isolate may provide us with new insights into the origins of the HIV-1 family.

L11 ANSWER 15 OF 18 MEDLINE
95111648 Document Number: 95111648. PubMed ID: 7812466. [Anti-HIV antibody screening kits and the difficulties of serology. Retrovirus Working Group of the Societe Francaise de la Transfusion Sanguine]. Trousses de depistage des anticorps anti-VIH et les difficultes de la serologie. Groupe de travail "Retrovirus" de la SFTS. Courouce A M. TRANSFUSION CLINIQUE ET BIOLOGIQUE, (1994) 1 (5) 387-95. Ref: 16. Journal code: 9423846. ISSN: 1246-7820. Pub. country: France. Language: French.

AB The combined HIV1 + HIV2 assays allow to screen simultaneously the subjects infected by HIV1 or by HIV2 (About 80 HIV1 for 1 HIV2 in blood donations in France). An improvement of both sensitivity and specificity was obtained by using artificial proteins which have been selected for having the most immuno-dominant epitopes. The sensitivity is defined by the study of samples from recent and very recent seroconverters and the specificity by testing 2000 unselected blood donors. All the early seroconversions must be recognized as positive and less than 0.5% false positive results must be found in blood donors. HIV1 variants, temporarily named sub-type O have brought a new difficulty to the HIV serology, due to a weak homology, especially in "env" domains, between these variants and the reference HIV1 strains. Subjects living in France and infected by this HIV1 variant seem rare and the screening assays which miss some of these infected individuals seem capable to modify their reagents in order to recognize all of them.

L11 ANSWER 10 OF 18 MEDLINE
97001626 Document Number: 97001626. PubMed ID: 8844618. Evaluation of a new third generation anti-HIV-1/anti-HIV-2 assay with increased sensitivity for HIV-1 group O. van Binsbergen J; de Rijk D; Peels H; Dries C; Scherders J; Koolen M; Zekeng L; Gurtler L G. (Organon Teknika, Boxtel, The Netherlands.) JOURNAL OF VIROLOGICAL METHODS, (1996 Jul) 60 (2) 131-7. Journal code: 8005839. ISSN: 0166-0934. Pub. country: Netherlands. Language: English.

AB Although the HIV-1 group O virus found in two persons of Cameroonian origin has been described in 1990 (De Leys et al., 1990), sera

from group O infected individuals became available only recently. Several studies showed that some of the anti-HIV-1/HIV-2 screening tests failed to detect all of these samples (Loussert-Ajaka et al., 1994; Simon et al., 1994; Schable et al., 1994; Gurtler et al., 1995). In the current version of an anti-HIV-1/anti-HIV -2 screening assay, namely the Vironostika HIV Uni-Form II, an HIV-O specific peptide was introduced in order to improve HIV-1 group O reactivity. The peptide was derived from the immunodominant region of HIV-1 group O gp41 strain ANT70 . All 30 anti-HIV-1 group O sera were detected by the so-called plus O assay, while 29 samples of this panel were positive the current assay. The sensitivity of the plus O assay for anti-HIV-1 and anti-HIV-2 positive samples is identical to that of the reference test without HIV-1 group O peptide. The clinical specificity of the HIV Uni-Form II plus O assay is improved to > or = 99.92% by an adjustment of the coat concentration of HIV-1 p24 (to avoid false positive p24 only reactions) without affecting sensitivity of the assay. The specific reaction of an HIV-1 group O specific rabbit serum for quality control purposes is presented.

L11 ANSWER 9 OF 18 MEDLINE
97407537 Document Number: 97407537. PubMed ID: 9264286. Envelope sequence variability and serologic characterization of HIV type 1 group O isolates from equatorial guinea. Hunt J C; Golden A M; Lund J K; Gurtler L G; Zekeng L; Obiang J; Kaptue L; Hampl H; Vallari A; Devare S G. (AIDS Research and Retrovirus Discovery, Abbott Laboratories, North Chicago, Illinois 60064, USA.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (1997 Aug 10) 13 (12) 995-1005. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Four sera from Equatorial Guinea (EG) suspected to contain antibody against HIV-1 group O-related viruses were identified on the basis of unusual and differential serologic reactivity in selected commercial assays and Western blot. Degenerate primers, designed from HIV-1 group O published sequences, were used to PCR amplify envelope (env) gene sequences from the suspect EG sera. A complete envelope gene sequence from each serum was determined from the overlapping env gene fragments. Analysis (PHYLIP package of programs) of Env amino acid sequences (translated from nucleotide sequences) indicated that the amino acid sequences obtained from EG sera clustered more closely with HIV Env sequences of group O compared to group M. The amino acid sequences at the octameric tip of the V3 loop were either RIGPLAWY (one isolate), RIGPMAWY (two isolates), or GLGPLAVY (one isolate). The V3 tip tetrameric sequence GPLA is represented only once in the 1995 HIV (Los Alamos) database, but was present in two of our group O-related EG samples. The gp41 immunodominant regions (IDR) protein sequences were identical for sequences from three of the sera, RLLALETLIQNQQLLNLWGCKGR(K)L(I)VCYTSVK(T)W, whereas sequence from the fourth serum contained three changes as noted in parentheses. IDR sequences derived from EG sera were unique compared to those reported for other HIV-1 group O isolate ANT70, VAU, or MVP5180.
Antibody in each EG serum directed against the IDR could be detected using synthetic peptides comprising sequences from the ANT70 or MVP5180 IDRs, but were most reactive against the sequences derived from the samples themselves. Little or no serologic reactivity was detected when EG sera were reacted against peptides comprising the IDR of HIV-1 group M (subtype B consensus) or HIV-2 (consensus).

L11 ANSWER 8 OF 18 MEDLINE
97418745 Document Number: 97418745. PubMed ID: 9274821. Diversity of the

immunodominant epitope of gp41 of HIV-1 subtype O and its validity for antibody detection. Eberle J; Loussert-Ajaka I; Brust S; Zekeng L; Hauser P H; Kaptue L; Knapp S; Damond F; Saragosti S; Simon F; Gurtler L G. (Pettenkofer Institute, University of Munchen, Germany.) JOURNAL OF VIROLOGICAL METHODS, (1997 Aug) 67 (1) 85-91. Journal code: 8005839. ISSN: 0166-0934. Pub. country: Netherlands. Language: English.

AB The immunodominant regions of the gp41 from 13 HIV-1 subtype O strains from Cameroon, 11 from France and one from Germany were sequenced. The amino acid sequences were compared to those of the 3 published HIV-1 subtype O isolates, ANT70, MVP-5180 and VAU. All HIV-1 subtype O isolates had a very conserved amino acid sequence in this region and showed a subtype O specific structure. Within the cysteine loop there was a positive charge of two basic amino acids, arginine and lysine. Only two strains (CM.6778 and CM.8161) showed an acidic amino acid in this loop. None of the isolates showed the same amino acid sequence in this immunodominant region. A 25 residue peptide from the immunodominant domain of gp41 of the MVP-5180 strain was synthesized, cycled to form the cysteine-loop and coated to microtiter plates. Antibody binding was detected by indirect ELISA using an enzyme labeled anti-human IgG. Out of 111 anti-HIV-1 positive specimens, collected mainly from Cameroonian HIV infected patients, only 10 were not reactive in this assay. The 42 anti-HIV-1 subtype O positive specimens gave all a reaction above cut off. Despite the diversity found in the amino acid sequences within the 25 isolates a peptide-based indirect ELISA representing the immunodominant epitope of the strain MVP-5180 successfully detected all the anti-HIV-O sera so far tested, pointing to the importance of adding such a peptide for correct identification of HIV-1 subtype O infected patients, while some assays without HIV-O specific antigens partially fail to detect all anti-HIV-O specimens.